REMARKS

Reconsideration of this application is respectfully requested.

Claims 240-282 are pending in this application. Claim 240 has been amended above. Claims 275-277 have been cancelled in favor of new claim 283. Claims 262-263 have also been cancelled without prejudice or disclaimer to Applicants' right to pursue the subject matter of these claims in a duly filed continuation or divisional application. No other claims have been amended, added, or cancelled by this Amendment. Accordingly, claims 240-261, 264-274 and 278-283 are presented for further examination.

Applicants and their attorney acknowledge the indication that the claims have been renumbered. Any inconvenience caused by the original misnumbering is sincerely regretted.

The title of the invention has been amended pursuant to the Examiner's direction. The new title is believed to be more descriptive of the instantly claimed invention.

The specification has been amended as follows. First, information updating patents and patent applications in the family has been inserted on pages 1 and 2 in the specification. Second, Applicants have deleted the portion of the specification beginning on page 4, line 1, through page 52, line 18. In this regard, Applicants and their attorney point out that it was an unfortunate act of draftsmanship that almost the entire contents of Ward et al., U.S. Patent No. 4,711,955, was copied verbatim and incorporated in that way into the originally filed specification. This contravened the more conventionally accepted practice of referring to the Ward et al. application (which later issued as the `955 patent) -- and incorporating it by reference into the instant application. In order to improve the readability of the specification, therefore, Applicants have hereinabove deleted the bulk of the Ward et al. disclosure from the specification at hand, while at the same time, maintaining the original language that incorporated by reference the disclosure and the publications cited therein. Third, minor typographical errors have been corrected in four instances (pages 66, 106 and

108). It is respectfully submitted that no new matter has been inserted by any of the foregoing amendments to the specification.

In an effort to define their invention more clearly, Applicants have amended the claims as follows. As now amended, claim 240 recites "[a] method of detecting a nucleic acid of interest in a sample, which method comprises the steps of (a) permitting hybridization of said nucleic acid of interest in the sample with an oligo- or polynucleotide . . ." Applicants have also deleted (without prejudice or disclaimer) the Markush elements (ii) and (iii) which they intend to pursue in a duly filed continuation and/or divisional application. Furthermore, step (b) in claim 240 now recites "detecting the presence of any of the oligo- or polynucleotides which have hybridized to said nucleic acid of interest." Claims 262-263 have been cancelled (without prejudice or disclaimer) in view of the deletion of the aforementioned Markush elements in claim 240. Finally, claims 275-277 have been cancelled in favor of new claim 283. Support for the latter new claim is found in the original disclosure (page 29, penultimate paragraph, through page 30 first paragraph). No new matter has been inserted by the foregoing amendments to the claims.

Applicants note the Examiner's remarks in the Office Action (page 2) that the PTO Form 1449 filed on June 28, 1993 was not executed nor was a copy enclosed since no copies of the references listed were filed. Applicants' attorney and his assistants are presently assembling art-related documents for inclusion into an Information Disclosure Statement Under 37 C.F.R. §§1.56 and 1.97-l.98. This IDS with complete copy of all documents will be submitted as soon as an indication has been received that the instant application has been revived.

The Rejection Under 35 U.S.C. §112, First Paragraph

Claims 240-282 stand rejected for limited enablement under 35 U.S.C. §112, first paragraph. In the Office Action (page 3) the Examiner stated that:

> . . . the disclosure is enabling only for claims limited to hybridization conditions that permit hybridization between the probe and target analyte. **[1]** The broad term "contacting" as cited, for example, in line 3 of claim 240 is not instantly supported beyond hybridization practice. **[2]** There is no instant disclosure or suggestion for analyte detection other than via hybridization practice as noted above. It is noted also that line 1 of claim 240 is broadly directed to "analyte" detection which is not

supported beyond nucleic acid target detection. **[3]** Also the last line of claim 240 cites the detection via "bound" practice. This also lacks instant support beyond "hybridized" practice. See M.P.E.P. §§ 706.03(n) and 706.03(z).

The Examiner further stated:

[4] Claims 275-277 also stand rejected under 35 U.S.C. §112, first paragraph, as the disclosure is enabling only for claims limited to antibiotic/bacterium species combinations that are instantly enabled. Not all possible combinations as suggested by these claims are instantly enabled. See M.P.E.P. §§706.03(n) and 706.03(z).

The rejection for limited enablement is respectfully traversed.

Referring to the bold bracketed numbers inserted above, Applicants offer the following remarks.

[1] The term "contacting" in line 3 of claim 240 has been replaced by the phrase "permitting hybridization of said nucleic acid of interest." In view of the substituted language, it is believed that this issue has been obviated.

[2] The amended preamble of claim 240 now recites "[a] method of detecting a nucleic acid of interest in a sample . . ." Step (b) has also been amended by substituting "nucleic acid of interest" for the term "analyte." It is believed that the foregoing changes obviate the second issue in this rejection.

[3] As noted above, the detection step (b) has been amended to recite the term "hybridized" instead of "bound." In view of this substitution, it is respectfully submitted that the third issue has been overcome.

[4] Regarding the antibiotic/bacterium species combinations, Applicants have deleted the rejected claims (275-277) in favor of new claim 283. New claim 283 corresponds to the now deleted original disclosure (page 29, penultimate paragraph, through page 30 first paragraph) and with the issued claim 37 in Ward et al., U.S. Patent No. 5,328,824 (issued on July 12, 1994). For the Examiner's convenience, a copy of the aforementioned Ward patent is attached hereto as Exhibit 1. Accordingly, new claim 283 corresponds to both the original disclosure (now deleted) as well as an already issued U.S. claim. In view of the above changes to the claims, the foregoing

remarks, and submitted Exhibit 1, Applicants respectfully request reconsideration and withdrawal of the fourth issue in the instant rejection.

The Rejection Under 35 U.S.C. §102(b)

Claims 240-244, 254-256, 259-263. 265. 267-273, 278, and 280 stand rejected under 35 U.S.C. §102(b) as being clearly allegedly anticipated by Kourilsky et al. [UK Patent Application GB 2,019,408A, published October 31, 1979]

In the Office Action (page 4), the Examiner stated:

> Kourilsky et al. disclose hybridization assay methods using RNA probes labeled with various label types such as disclosed on page 1, line 38-53. Antibody and enzyme label moieties are also disclosed by Kourilsky et al. for example on page 5, lines 18-20. Electron dense labels are disclosed via mercury as given on page 2, lines 47-52. It is noted that instant claim 240 cites Sig moieties linked either to the sugar moiety or phosphate moiety with minimal limitation as to the signal moiety as being detectable. Kourilsky et al. also cite a variety of targets inclusive of genetic diseases, bacterial infections, etc. Taken as a whole Kourilsky et al. reads on the broadly claimed instant invention.

The rejection for anticipation is respectfully traversed.

As noted above, Applicants have deleted without prejudice or disclaimer the Markush elements (ii) and (iii) in claim 240. The subject matter represented by these elements will be pursued in a future filing. Thus, the instantly claimed subject matter is directed to a detection method that utilizes a novel nucleotide in which the base has been disruptively or semi-disruptively modified with a detectable moiety Sig. In view of the above amendments to claim 240, Applicants respectfully request reconsideration and withdrawal of the anticipation rejection.

The First Rejection Under 35 U.S.C. §103

Claims 272-277 stand rejected under 35 U.S.C. §103 as being allegedly unpatentable over Kourilsky et al. taken in view of Falkow et al. [U.S. Patent No. 4,358,535, issued November 9, 1982, based on an application filed on December 8, 1980]

In the Office Action (pages 5-6), the Examiner stated:

> Kourilsky et al. discloses the basics of the instant invention but lacks specific antibiotic resistance gene target detection via hybridization assay but via its generic nucleic acid target disclosure supplies motivation and a reasonable expectation of success for generic nucleic acid targets.
>
> Falkow et al. disclose the detection of various bacterial targets via antibiotic resistance genes disclosed in the abstract as well as the disclosure as a whole.
>
> Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice hybridization assay detection of etiological agents via the bacterial antibiotic resistance genes because Kourilsky et al. discloses the basic detection methodology and Falkow et al. adds said antibiotic resistance genes of bacteria as nucleic acid targets having a reasonable expectation of success in such hybridization assays.

The obviousness rejection above is respectfully traversed.

As noted in the rejection under 35 U.S.C. §112 (first paragraph), Applicants are now pursuing subject matter in which the detection method utilizes a novel nucleotide in which the base is disruptively or semi-disruptively modified with a detectable Sig moiety. Applicants respectfully contend that Kourilsky et al. neither disclose nor suggest either the instantly recited nucleotide per se or a detection method that utilizes such, as set forth in the instant invention. Reconsideration and withdrawal of the rejection under §103 is respectfully requested.

The Second Rejection Under 35 U.S.C. §103

Claims 240-282 also stand rejected under 35 U.S.C. §103 as being allegedly unpatentable over Kourilsky et al. [GB 2,019,408 A]. In the Office Action (page 6), the Examiner stated:

> The instant invention broadly is directed to methods using a variety of covalent linkages between a generic "Sig" moiety and hybridization probes used to detect generic targets or wide scope.
>
> Kourilsky et al. discloses the basic hybridization assay using probes labeled in a variety of ways as discussed in the above rejections. It is noted that claim 240 cites "Sig" linkages to every portion of a

nucleotide residue only excluding very specific base moiety linkages. This broad "Sig" disclosure permits Kourilsky et al. to suggest Sig moieties that may be as simple as labeled segments of probes which may or may not participate in direct hybridization. Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the instant invention given a wide generic set of labels with Sig linked at least at one of the instantly claimed linkages given broad linkages as disclosed by Kourilsky et al.

As noted above in all three previous rejections, Applicants are now pursuing subject matter in which the detection method utilizes a novel nucleotide in which the base is disruptively or semi-disruptively modified with a detectable Sig moiety. Applicants respectfully contend that the cited documents, taken singly or in combination, do not disclose or suggest the instantly claimed subject matter. Reconsideration and withdrawal of the rejection under §103 is respectfully requested.

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SUMMARY AND CONCLUSIONS

Claims 240-261, 264-274 and 278-283 are presented for further examination.

This Amendment is accompanying as Exhibit B a Petition to Revive An Unintentionally Abandoned Application Under 37 C.F.R. §1.137(b) and authorization for the fee therefor. No fee is believed to be due for this Amendment itself. If any fee is due, however, for this Amendment, or other fee(s) are due for the Petition, The Patent and Trademark Office is authorized to charge the amount of any such fee(s) to Deposit Account No. 05-1135, and to credit any overpayment thereto.

In view of the above discussion of the issues and amendments to the claims, and the submitted exhibit, Applicants respectfully submit that all of the instant claims, 240-261, 264-274 and 278-283, are in allowable condition. Should it be deemed helpful or necessary, the Examiner is respectfully invited to telephone the undersigned at (212) 856-0876 to discuss the subject application.

Respectfully submitted,

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